

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FIRINFR ALTION	CTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT IPEA 416)		
P872 PCT International application No	International filing date <i>(day month)</i>			
PCT US00 16895	19 June 2000 (19.06.2000)	17 June 1999 (17.06.1999)		
International Patent Classification (IPC)		1 June 1777 (1 .00.1777)		
IPC(7): A01N 1 02 and US Cl.: 435 1.1	. 1.2			
Applicant				
THE REGENTS OF UNIVERSITY OF	CALIFORNIA			
 This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. This REPORT consists of a total of Asheets, including this cover sheet. 				
2. This REPORT consists of	a total of sneets, including thi	s cover sheet.		
This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).				
These annexes consist of a	$\frac{1}{2}$ total of $\frac{1}{2}$ sheets.			
3. This report contains indica	ntions relating to the following iter	ns:		
I Basis of the rep	ort			
II Priority				
III Non-establishm	ent of report with regard to novelt	y, inventive step and industrial applicability		
IV Lack of unity o				
V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement				
VI Certain documents cited				
VII Certain defects in the international application				
VIII Certain observations on the international application				
Date of submission of the demand	Date of	completion of this report		
10 January 2001 (10.01.2001)		ary 2002 (11.02.2002)		
Commissioner of Patents and Trademarks Box PC1 Washington, D.C. 2, 251		Sabcier Pully 2009		

Form PCT IPEA 409 (cover sheet)(July 1998)

International application No	
PCT US00 168	

I.	Bas	is of the report
:	Witt	regard to the elements of the international application.*
		the international application as originally filed.
		the description:
		pages 1-57 as originally filed
		pages NONE, filed with the demand, filed with the letter of
		the claims:
		pages <u>58</u> , as originally filed pages <u>NONE</u> , as amended (together with any statement) under Article 19
		pages NONE . filed with the demand
		pages NONE , filed with the letter of
		the drawings
		pages 1-5 , as originally filed
		pages NONE , filed with the demand pages NONE , filed with the letter of
		pages NONE, filed with the letter of
		the sequence listing part of the description:
		pages NONE as originally filed
		pages NONE, filed with the demand, filed with the letter of
2.	Wit	h regard to the language , all the elements marked above were available or furnished to this Authority in the
	lang	uage in which the international application was filed, unless otherwise indicated under this item.
	The	se elements were available or furnished to this Authority in the following language which is:
		the language of a translation furnished for the purposes of international search (under Rule23.1(b)).
		the language of publication of the international application (under Rule 48.3(b)).
		the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).
3.		h regard to any nucleotide and/or amino acid sequence disclosed in the international application, the
	inte	rnational preliminary examination was carried out on the basis of the sequence listing:
	L	contained in the international application in printed form.
		filed together with the international application in computer readable form.
		furnished subsequently to this Authority in written form.
		furnished subsequently to this Authority in computer readable form.
		The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
		The statement that the information recorded in computer readable form is identical to the written sequence listing
		has been furnished
4.	\times	The amendments have resulted in the cancellation of
		the description, pages none
		the claims, Nos. none
		the drawings, sheets fig none
5.		This report has been established as if (some of) the amendments had not been made, since they have been considered to go
` '		beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)) **
:h	is rep	acement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in ort as "originally filed" and are not annexed to this report since they do not contain amendments. (Rules 70.16 and 70.17) replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

	International application No
	mermatonal appropriate
	PCT US00 168
1	161 6300 10
1	

V.	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability.
	citations and explanations supporting such statement

1. STATEMENT Novelty (N) Claims 1 YESClaims 2.3 NO Inventive Step (IS) Claims NONE YES Claims 1-3 NO Industrial Applicability (IA) Claims 1-3 YES Claims NONE NO 2. CITATIONS AND EXPLANATIONS Claim 2 lacks novelty under PCT Article 33(2) as being anticipated by WINSLOW (US 5,814,601). The claim is drawn to a solution for organ preservation comprising PEG coated bovine hemoglobin. US 5.814.601 discloses hemoglobin from bovine origins coated with PEG (col. 11, lines 18 and 28). Claims 2 and 3 lack novelty under PCT Article 33(2) as being anticipated by Nakajima et al. Claim 2 has been discussed above and claim 3 is drawn to a composition further comprising and oxygen, nutritional and electrolyte environment. Nakajima et al. disclose a composition comprising hemoglobin and polyoxyethylene in a solution with glucose and electrolytes (page 277. Materials and Methods and Table 1) which creates an oxygen, nutritional and electrolyte environment. Claim 1 lacks an inventive step under PCT Article 33(3) as being obvious over SEGEL (US 5,374,624) in view of STRASBERG et al. (US 5,200,398). The claim is drawn to a composition for organ preservation comprising PEG-Hb, human albumin, dextrose, sodium heparin, lidocaine HCL, MgSO4, KCl, CaCl2, THAM, NaCl, NaHCO3 and Na3PO4. US 5.374,624 discloses a composition comprising fluorochemicals, albumin, dextrose, sodium heparin, lidocaine, MgCl2, KCl, CaCl2, NaCl, NaHCO3 and KH2PO4. This composition lacks the inclusion of THAM and SO4 ion. All other ions of the claimed solution are present in the solution of the reference. Many crystalloid solutions used for organ preservation such as Eurocollins' solution have Mg2SO4 as the magnesium salt instead of MgCl2. As no criticality has been demonstrated, the use of Mg2SO4 as a substitute for MgCl2 is considered to be the substitution of equivalents and both have been used in preservative solutions as shown in US 5,200,398 (Table 1). With regard to the inclusion of THAM, this is a conventional biological buffer and its addition to a solution in order to stabilize pH cannot be considered to be inventive. ----- NEW CITATIONS -----US 5,200,398 A (STRASBERG et al.) 06 April 1993, see Table 1

International appropriate No. PCT US00-16

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Section I. Basis of the report, Item 5

The amendment of the description claim filed 25 June 2001 is objected to under PCT Article 34(20b) because it adds matter into the application that goes beyond the disclosure as originally filed. The added matter which is new is as follows. On 25 June 2001, amendments were submitted to claims disclosure figures under Article 19. However, Article 19 amendments are only made to the claims during the search phase. Thus, the amendments to the description and figures under Article 19 were improper. Also, as the demand was filed 10 January 2001 and the written opinion (408) was mailed 18 May 2001, the application was not in the search phase. Thus, the amendments to the claims under Article 19 was also improper and no amendments under Article 19 have been entered. Further, on 25 June 2001, an amendment to the description and figures was submitted under Article 34. However, it has not been entered because of new matter. For example, in the amended abstract, the perfusion solution comprises Na2HPO4 NaH2PO4, while in the original abstract, the perfusion solution comprises Na3PO4. Another example is the amended abstract states that the invention comprises polyethylene CONJUGATED hemoglobin, while the original abstract states that the invention comprises polyethylene CONJUGATED hemoglobin. This is a change in both the scope of the invention and the substance of the statement of the invention as a conjugated chemical composition differs in structure from one which is a coated composition as coating does not require conjugation. Extensive amendments to the figures description under Article 34 have not been entered as they introduce new matter by changing the scope and substance of the disclosure.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/16895

V. Reasoned statement under Rule 66.2(a)(ii) with recitations and explanations supporting such statem	gard to novelty, inventive step or industrial applicability;
1. STATEMENT	
Novelty (N) Clai	ms 1 YES
	ns <u>2.3</u> NO
Inventive Step (IS) Clar	ns NONE YES
_	
Industrial Applicability (IA) Clay	ne 1.2 VES
1	
Industrial Applicability (IA) Claims 1-3 YES	

Form PCT/IPEA/409 (Box V) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/16895

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Section I. Basis of the report, Item 5

The amendment of the description/claim filed 25 June 2001 is objected to under PCT Article 34(2)(b) because it adds matter into the application that goes beyond the disclosure as originally filed. The added matter which is new is as follows: On 25 June 2001, amendments were submitted to claims/disclosure/figures under Article 19. However, Article 19 amendments are only made to the claims during the search phase. Thus, the amendments to the description and figures under Article 19 were improper. Also, as the demand was filed 10 January 2001 and the written opinion (408) was mailed 18 May 2001, the application was not in the search phase. Thus, the amendments to the claims under Article 19 was also improper and no amendments under Article 19 have been entered. Further, on 25 June 2001, an amendment to the description and figures was submitted under Article 34. However, it has not been entered because of new matter. For example, in the amended abstract, the perfusion solution comprises Na2HPO4/NaH2PO4, while in the original abstract, the perfusion solution comprises Na3PO4. Another example is the amended abstract states that the invention comprises polyethylene CONJUGATED hemoglobin, while the original abstract states that the invention and the substance of the statment of the invention as a conjugated chemical composition differs in structure from one which is a coated composition as coating does not require conjugation. Extensive amendments to the figures/description under Article 34 have not been entered as they introduce new matter by changing the scope and substance of the disclosure.

Form PCT/IPEA/409 (Continuation Sheet) (July 1998)



From the

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

DANIEL L. DAWES MYERS, DAWES & ANDRAS LLP 650 TOWN CENTER DRIVE SUITE 650 COSTA MESA. CA 92626

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing 0 6 MAR 2002 (day month year) Applicant's or agent's file reference IMPORTANT NOTIFICATION P872 PCT International filing date (day month year) Priority date (day month year) International application No. PCT US00 16895 19 June 2000 (19.06.2000) 17 June 1999 (17.06.1999) Applicant THE REGENTS OF UNIVERSITY OF CALIFORNIA

- The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA US

Commissioner of Patents and Trademarks

R & PCT

Washington, D.C., 2, 231

Facsimile No. (703)305-3230 Form PCT IPEA 416 (July 1992)

Telephone No. (703) 308-019.

INTERNATIONAL SEARCH REPORT

International application No.

S00/16895

A. CLASSIFICATION OF SUBJECT MATTER			
IPC(7) :A01N 1/02			
	:435/1.1, 1.2 to International Patent Classification (IPC) or to both	national classification and IPC	
	LDS SEARCHED	-d by all afficient anniholo)	
Minimum d	ocumentation searched (classification system followed	ed by classification symbols)	
U.S . :	435/1.1, 1.2		
Documenta	tion searched other than minimum documentation to th	e extent that such documents are included	in the fields scarched
T71	data base consulted during the international search (n	and of data base and subare practicable	e search terms used)
		ane of data base and, where practicable	c, scarch willis used)
Ca on line	e, USPATFULL, Medline, Biosis		
C. DOC	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.
x	US 5,814,601 A (WINSLOW et al.) 29	September 1998, col. 11 and	2
	12.		1.0
Y			1,3
Y	US 5,374,624 A (SEGEL) 20 Decemb	per 1994, Table 1.	1-3
	, ,		
X	NAKAJIMA et al. Forty-eight hour	liver preservation using an	2,3
	artificial blood substitute. Asaio Transa		
	No. 3, pages 277-279, especially Tabl	e 1.	
Furth	er documents are listed in the continuation of Box C	Sec patent family annex.	
• Spe	scial cetegories of cited documents:	"T" later document published after the inte date and not in conflict with the appl	
	rument defining the general state of the art which is not considered be of perticular relevance	the principle or theory underlying the	na ention
.E. est	iser document published on or after the international filing date	 "X" document of particular relevance, the considered novel or cannot be consider 	
	sument which may throw doubts on priority claim(s) or which is do to establish the publication date of another citation or other	when the document is taken alone	
•	cial reason (as specified)	"Y" document of particular relevance, the considered to involve an inventive	step when the document is
=•		combined with one or more other such being obvious to a person skilled in t	he art
P document published prior to the international filing date but later than *& document member of the same patent family the priority date claimed			
Date of the	Date of the actual completion of the international search Date of mailing of the international search report		
23 AUGU	23 AUGUST 2000 2 0 SEP 2000		
	nailing address of the ISA/US	Authorized officer Rife	bruch
Commission Box PCT	Commissioner of Patents and Trademarks Box PCT SANDRA SAUCIER		
Washington	L. D.C. 20231	J	g~
Faceimile N	o (703) 305-3230	Telephone No. (703) 308-0196	\



From the INTERNATIONAL SEARCHING AUTHORITY

To: DANIEL L. DAWES MYERS, DAWES & ANDRAS LLP 650 TOWN CENTER DRIVE, SUITE 650	PCT	
COSTA MESA, CA 92626	NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION	
	(PCT Rule 44.1)	
	Date of Mailing (day/month/year) 20 SER 2000	
Applicant's or agent's file reference	FOR FURTHER ACTION See paragraphs 1 and 4 below	
NONE	International Glina data	
International application No.	International filing date (day/month/year) 19 JUNE 2000	
PCT/US00/16895	19 JUNE 2000	
Applicant REGENTS OF THE UNIVERSITY OF CALIFORNIA		
1. X The applicant is hereby notified that the internationa	il search report has been established and is transmitted herewith.	
Filing of amendments and statement under Artic	le 19:	
**	the claims of the international application (see Rule 46): tents is normally 2 months from the date of transmittal of the	
	r more details, see the notes on the accompanying sheet.	
Where? Directly to the International Bureau of V 34, chemin des Colombe 1211 Geneva 20, Switze Facsimile No.: (41-22) 7	ettes rland	
For more detailed instructions, see the notes on the accompanying sheet.		
2. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.		
3. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:		
the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.		
no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.		
4. Further action(s): The applicant is reminded of the following	llowing:	
Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.		
Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).		
Within 20 months from the priority date, the applicant m	ust perform the prescribed acts for entry into the national phase and in the demand or in a later election within 19 months from the	
Name and mailing address of the ISA/US	Authorized officer	
Commissioner of Patents and Trademarks Box PCT	SANDRA SAUCIER	
Washington, D.C. 20231	1 M	

(703) 308-0196

Telephone No.



INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference NONE		Transmittal of International Search Report 20) as well as, where applicable, item 5 below.			
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)			
PCT/US00/16895	19 JUNE 2000	17 JUNE 1999			
Applicant REGENTS OF THE UNIVERSITY O	Applicant REGENTS OF THE UNIVERSITY OF CALIFORNIA				
This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau. This international search report consists of a total of $\frac{2}{2}$ sheets.					
X It is also accompanied by a	copy of each prior art document cited in this	report.			
language in which it was filed the international search wa Authority (Rule 23.1(b)). b. With regard to any nucleotide was carried out on the basis of contained in the internation filed together with the internation of the subsequently to the statement that the subsequently to the statement that the informational application as the statement that the informational contained. Certain claims were found Unity of invention is lacked. With regard to the title,	of the sequence listing: nal application in written form. rnational application in computer readable for this Authority in written form. Authority in computer readable form. Equently furnished written sequence listing doe filed has been furnished. nation recorded in computer readable form is ide d unsearchable (See Box I). Ling (See Box II).	the international application furnished to this international application, the international search m.			
5. With regard to the abstract,					
X the text is approved as sub	* **				
the text has been established Box III. The applicant may search report, submit come	ed, according to Rule 38.2(b), by this Authorit, within one month from the date of mailing of ments to this Authority.	y as it appears in this international			
6. The figure of the drawings to be	published with the abstract is Figure No.				
as suggested by the application	ant.	X None of the figures.			
because the applicant failed	d to suggest a figure.				
because this figure better of	characterizes the invention.				

A. CLASSIFICATION OF SUBJECT MATTER			
IPC(7) :A01N 1/02 US CL :435/1.1, 1.2			
	o International Patent Classification (IPC) or to both	national classification and IPC	
	DS SEARCHED ocumentation searched (classification system followe	ad by alaccification cymbols)	
	435/1.1, 1.2	ed by classification symbols)	
Documentat	ion searched other than minimum documentation to the	e extent that such documents are included	in the fields searched
	data base consulted during the international search (ne, USPATFULL, Medline, Biosis	ame of data base and, where practicable	e, search terms used)
C. DOC	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.
X	US 5,814,601 A (WINSLOW et al.) 29	September 1998, col. 11 and	2
Y	12.		1,3
Y	US 5,374,624 A (SEGEL) 20 Decemb	per 1994, Table 1.	1-3
X	NAKAJIMA et al. Forty-eight hour liver preservation using an artificial blood substitute. Asaio Transactions. Jul-Sep 1988, Vol. 34, No. 3, pages 277-279, especially Table 1.		
Further documents are listed in the continuation of Box C. See patent family annex.			
"A" doc	ecial categories of cited documents cument defining the general state of the art which is not considered be of particular relevance	"T" later document published after the inte date and not in conflict with the appl the principle or theory underlying the	ication but cited to understand
	lier document published on or after the international filing date	"X" document of particular relevance, the considered novel or cannot be considered.	
cité	cument which may throw doubts on priority claim(s) or which is dd to establish the publication date of another citation or other icial reason (as specified)	when the document is taken alone *Y* document of particular relevance, the	
O doc	cument referring to an oral disclosure, use, exhibition or other ans	considered to involve an inventive combined with one or more other such being obvious to a person skilled in the control of th	documents, such combination
	cument published prior to the international filing date but later than priority date claimed	"&" document member of the same patent	family
·		Date of mailing of the international sea	arch report
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 Authorized officer SANDRA SAUCIER Telephone No. (703) 308-0196		andy.	

We claim:

1	 A composition for donor organ preservation for transplantation
2	comprising an ischemic hypothermic immersion saline solution including PEG-Hb,
3	human albumin, dextrose, heparin sodium, lidocaine HCl, MgSO₄, KCl, CaCl₂,
4	THAM, NaCl, NaHCO3, and Na ₃ PO ₄ .

- 1 2. A composition for donor organ preservation for transplantation 2 comprising a polyethylene glycol coated bovine hemoglobin based solution for the 3 purpose of ex vivo donor organ preservation to preserve donor human and animal 4 organs, *ex vivo*, prior to transplantation.
- 1 3. A composition for donor organ preservation for transplantation comprising an oxygen, nutritional and electrolyte environment to tissue of the donor organ to provide *ex vivo* preservation such that the donor organ will regain acceptable function post transplantation.